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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,889	06/05/2006	Achim Feurer	Le A 36 411	5900
35969	7590	03/14/2008		
Bayer Health Care LLC 400 Morgan Lane West Haven, CT 06516			EXAMINER MURRAY, JEFFREY H	
			ART UNIT 1624	PAPER NUMBER
			MAIL DATE 03/14/2008	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/531,889

Applicant(s)

FEURER ET AL.

Examiner

JEFFREY H. MURRAY

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 10 December 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 8-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 8-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)
- Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. This action is in response to a non-final rejection filed on December 10, 2007. There are eight claims pending and eight claims under consideration. Claims 5-7 have been cancelled. This is the second action on the merits. The present invention relates to heteroaryloxy-substituted phenylaminopyrimidines, to a process for their preparation and to their use for preparing medicaments for the treatment and/or prophylaxis of diseases in humans and animals, in particular cardiovascular disorders.

Status of Objections

2. The specification was objected to for lacking the preferred layout as set forth in CFR 1.77(b). Applicants have chosen not to follow the preferred layout, which is not mandatory. Therefore, the objection to the specification is hereby withdrawn.

Status of Rejections

3. Claims 8 and 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The amendments made by the applicants have been noted, but have not been found persuasive, therefore the rejection of Claims 8 and 11 are hereby upheld.

4. Claims 1-4 and 8-11 are rejected under nonstatutory obviousness-type double patenting as being unpatentable over Claims 1, 4, 8-10 and 12 of U.S. Application No. 11/547,975. Applicants' have asked this rejection be held in abeyance until the claims are in allowance but for this rejection. As such, the rejection is hereby upheld.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Upheld/New Rejections

Claim Rejections - 35 USC § 112, 1st paragraph

5. Claims 8 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating the cardiovascular disease erectile dysfunction, does not reasonably provide enablement for the prophylaxis of erectile dysfunction or any other cardiovascular disorder. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

6. Examiner has rejected these claims in part due to their use of the term "prophylaxis" and in part due to their use of the term cardiovascular disorders. The use of the term "prophylaxis" is not permitted in claim language unless applicant can show that the method is 100% effective. The term "prophylaxis" means, "Prevention of disease or of a process that can lead to disease measure taken for the 'prevention' of a disease or condition." (<http://www.thomsonhc.com/pdrel/librarian/PFDefaultActionId/pdrcommon.Stedmans>) (cited in last action). Applicant must show that the claimed method "prevents" a cardiovascular disorder in all instances and in all situations. The specification fails to fully enable the claimed compound for the prevention of a cardiovascular disorder. The term "prevent" encompasses the ability of the specific antigen to induce protective immunity to any cardiovascular disorder. Many people cannot prevent cardiovascular disease because they are born with a genetic predisposition. (<http://heartcenter.uc.edu/global.cfm?SecId=Cardiology>). (cited in previous action).

The human genome is a sequence of 3 billion base pairs, over 100,000 genes organized along the chromosomes. These genes come in different forms called alleles. Differences in alleles arise from mutations in the base pairs. Although mutations in genes have a possibility of being indifferent or advantageous they are notorious for their ability to lead to disease or susceptibility for disease. In cardiovascular diseases, over 5% of all cataloged genes have some affect on the heart while hundreds of genes are

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expected to be essential for normal development and physiology of the cardiovascular system. Up to 50% of patients with extreme mutations die by the age of 40. Most forms of heart disease appear to have three components with varying amounts of importance depending on the disease: 1) environmental risk factors; 2) ***genetic (or inherited) risk factors***; and, 3) chance.

There are a number of known risk factors that themselves have recognized genetic components such as diabetes, hypertension, high cholesterol (hypercholesterolemia) and hyperlipidemia and there are also genes that increase one's risk of heart disease such as homocysteine (homocystinemia), fibrinogen, Apolipoprotein E, and Apolipoprotein B.

Most cardiovascular diseases are a result of multiple abnormalities in many different genes on several chromosomes (polygenic) with no clear phenotypic differences. Hypertension is one an example – where up to 20 genes are presumed to be related to hypertension. Others are the renin-angiotensin system, kallikrein system, nitrous oxide system, membrane (ion) channels, catecholamines, cardiovascular peptide, and neuropeptides. (http://www.musc.edu/bmt737/Spr_1999/gizelle/heart.html)

It is quite clear that if genetics plays such a large role in a number of cardiovascular diseases, that the applicant could not possibly prophylax or “prevent” a disease or of a process that can lead to disease measure taken for the ‘prevention’ of a disease or condition, when many cardiovascular diseases are genetic in nature to begin with.

Likewise when it comes to the disease of erectile dysfunction, there are also "other factors" that must be considered. The specific steps take place to produce and sustain an erection are the 1) arousal, or the first step is sexual arousal, which men obtain from the senses of sight, touch, hearing and smell, and from thoughts; 2) the nervous system response when the brain communicates the sexual excitation to the body's nervous system, which activates increased blood flow to the penis, and finally, the blood vessel response where a relaxing action occurs in the blood vessels that supply the penis, allowing more blood to flow into the shafts that produce the erection. If something affects any of these factors or the delicate balance among them, erectile dysfunction can result.

The two types of causes are nonphysical causes and physical causes. Among the nonphysical causes may include psychological problems, the most common of which are stress, anxiety and fatigue. Impotence is also an occasional side effect of psychological problems such as depression. Another is negative feelings. Feelings that you express toward your sexual partner — or that are expressed by your sexual partner — such as resentment, hostility or lack of interest also can be a factor in erectile dysfunction.

Physical causes account for many cases of erectile dysfunction and among them may include: nerve damage from longstanding diabetes (diabetic neuropathy), cardiovascular disorders affecting the blood supply to the pelvis, certain prescription medications, operations for cancer of the prostate, fractures that injure the spinal cord, multiple sclerosis, hormonal disorders, and alcoholism and other forms of drug abuse.

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In fact, erectile dysfunction may be one of the first signs of an underlying medical problem.

The physical and nonphysical causes of erectile dysfunction commonly interact. For instance, a minor physical problem that slows sexual response may cause anxiety about attaining an erection. Then the anxiety can worsen your erectile dysfunction.

<http://www.cnn.com/HEALTH/library/DS/00162.html>

A wide variety of physical and emotional risk factors can contribute to erectile dysfunction. They include physical diseases and disorders, surgery or trauma, medications, substance abuse, stress, anxiety or depression.

Physical diseases and disorders such as chronic diseases of the lungs, liver, kidneys, heart, nerves, arteries or veins can lead to impotence. So can endocrine system disorders, particularly diabetes. The accumulation of deposits (plaques) in your arteries (atherosclerosis) also can prevent adequate blood from entering the penis. And in some men, erectile dysfunction may be caused by low levels of the hormone testosterone (male hypogonadism). Surgery or trauma can cause damage to the nerves that control erections and can lead to erectile dysfunction. It may result from an injury to the pelvic area or spinal cord. Surgery to treat bladder, rectal or prostate cancer also can result in erectile dysfunction. Prolonged bicycle riding also can cause a temporary problem. A wide range of drugs such including antidepressants, antihistamines and medications to treat high blood pressure, pain and prostate cancer can cause erectile dysfunction by interfering with nerve impulses or blood flow to the penis. Tranquilizers and sleeping aids also may pose a problem. Substance abuse

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such as the chronic use of alcohol, marijuana or other drugs often causes erectile dysfunction and decreased sexual drive. Excessive tobacco use also can damage penile arteries. Finally, the stress, anxiety or depression or other similar psychological conditions can contribute to some cases of erectile dysfunction.

<http://www.cnn.com/HEALTH/library/DS/00162.html>

As seen above, the applicants cannot “prophylax” a cardiovascular disease without addressing all of the previously mentioned issues. While it may be possible for the applicants to treat some cardiovascular diseases, it is not possible for applicants to “prevent” all cases of cardiovascular diseases. In addition, it is also not feasible for applicants to be capable of treating erectile dysfunction in all instances. (i.e. a case where there is nerve damage). “In the disorder of erectile dysfunction, in most cases, it cannot be cured, but, in many cases; it can be treated effectively.”

(<http://www.allabouted.com.my/english/understanding/faqs.html>). (previously presented)

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

7. Claims 1-4 and 8-11 are rejected under nonstatutory obviousness-type double patenting as being unpatentable over Claims 1, 4, 8-10 and 12 of U.S. Application No. 11/547,975. Applicants' have asked this rejection be held in abeyance until the claims are in allowance but for this rejection. As such, the rejection is hereby upheld.

Conclusion

8. Claims 1-4 and 8-11 are rejected.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is 571-272-9023. The examiner can normally be reached on Mon.-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/
Patent Examiner
Art Unit 1624

**/James O. Wilson/
Supervisory Patent Examiner Art
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